HIV-1 Incidence, Adherence to Ring Use and Safety in an Open-label Trial of Dapivirine Vaginal Ring - DREAM

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Background:
DREAM is an ongoing Phase IIIb, multi-center, open-label follow-on trial to The Ring Study, a Phase III trial of the monthly Dapivirine Vaginal Ring (25 mg), to evaluate continued safety and adherence to ring use. All participants who had previously participated in The Ring Study and were HIV-negative, and not pregnant or breastfeeding at screening for DREAM, were eligible for enrollment.

Methods:
1034 women who participated in The Ring Study were screened, and 941 were enrolled at 5 Research Centers (RCs) in South Africa and 1 in Uganda. All enrolled participants use the monthly Dapivirine Vaginal Ring. Monthly RC visits occur up to 3 months after enrolment, followed by quarterly visits for a study period of approximately 12 months.

HIV testing and safety evaluations are conducted at each visit, and returned used rings are analyzed for dapivirine residual levels. The observed HIV-1 incidence rate was compared descriptively to the rate expected by bootstrap sampling, based on the placebo arm of The Ring Study, selecting 10,000 times for a subset of women matched for research center, age, and presence of a curable sexually transmitted infection at enrollment.

A total of 1054.1 person-years of follow-up have been reported up to 30 April 2018. An expected 100 additional person-years will be accrued until the planned completion of the trial by end 2018.

Results:
- By 30 April 2018, 571 (61%) completed. 47 (7%) discontinued early and 302 (32%) participants were ongoing.
- The observed HIV-1 incidence rate is 1.61 per 100 person-years (95% CI: 0.94 to 2.48).
  - HIV-1 seroconversion occurred in 26 participants; 17 were infected while using Dapivirine Vaginal Ring.
  - Although interpretation of the data is limited by the lack of a placebo arm, the rate is approximately 59% lower than the expected rate (3.92 per 100 person-years; 95% CI: 2.99 to 4.93 based on bootstrap analysis) in the absence of access to the Dapivirine Vaginal Ring.
  - Dapivirine residual levels in used rings are consistently lower in DREAM compared to The Ring Study: 96% of returned used rings had a residual level ≤ 2.35 mg, indicating some ring use during the month, compared to 83% in The Ring Study.
  - Overall, most of the participants self-reported adherence to ring use to be in the ≥ 90% category.
- DREAM results indicate a similar safety profile to that observed in the Phase III trials:
  - SAEs were reported for 20 (2.1%) participants; no SAEs or AEs led to permanent discontinuation of ring use.
  - Pregnancies occurred in 26 (2.8%) participants.
  - Social harms were reported by 24 (2.5%) participants.

Conclusion:
The HIV-1 incidence rate is approximately 59% lower than the expected rate in the absence of Dapivirine Vaginal Ring use. The lack of a placebo arm limits interpretation but increased efficacy can be expected due to observed higher adherence to ring use in DREAM than in Phase III. DREAM demonstrates a similar safety profile of Dapivirine Vaginal Ring to that observed in Phase III.